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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,752	04/08/2005	Shuh Narumiya	Q87373	7330

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EXAMINER

GRAFFEO, MICHEL

ART UNIT PAPER NUMBER

1614

DATE MAILED: 04/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/530,752

Applicant(s)

NARUMIYA, SHUH

Examiner

Michel Graffeo

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 8-15 is/are pending in the application.
- 4a) Of the above claim(s) 7 and 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 8-15 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

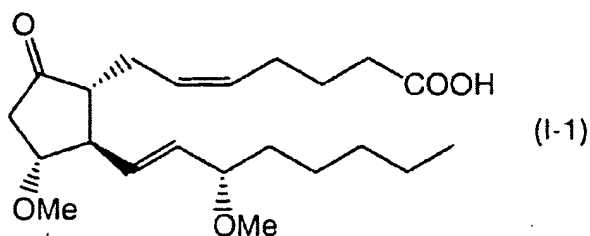
Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>7/7/05; 4/8/05</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of the following compound:



in the reply filed on 24 February 2006 is acknowledged.

Claims 7 and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Status of Action

Applicant has amended claim 5 and added claims 11-16 in the response filed 24 February 2006. Claims 1-6 and 8-15 are pending and examined.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

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Claim 10 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The phrases "Use of" and "The use of" constitute non-statutory claim language. However, in order to advance prosecution these claims will be examined as method of use claims.

Claim 10 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). It is incumbent upon Applicant to properly amend the claim(s) to be in proper process of use format.

Claim Rejections - 35 USC § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a mouse asthma model with the elected compound to the extent that the number of eosinophils and neutrophils decreased does not reasonably provide enablement for the treatment and/or prevention of all allergic diseases nor for the treatment without any specified endpoint with any EP3

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receptor agonist for each and every mammalian patient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2nd 1400 (Fed. Cir. 1988) as to undue experimentation.

The factors include:

- 1) the nature of the invention;
- 2) the breadth of the claims;
- 3) the predictability or unpredictability of the art;
- 4) the amount of direction or guidance presented;
- 5) the presence or absence of working examples;
- 6) the quantity of experimentation necessary;
- 7) the state of the prior art; and ,
- 8) the relative skill of those skilled in the art.

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the art in the assessment of undue experimentation.

- 1) the nature of the invention; the invention is directed to an anti-allergy therapy and method of treating and preventing allergic disease but has not recited the step(s) that (a) result in preventing nor (b) have a specified end result of the treatment.
- 2) the breadth of the claims; the scope of the method claims includes the prevention and/or treatment of all allergies with any EP3 receptor agonist.
- 3) the predictability or unpredictability of the art; the ability of preventing all allergic diseases is not yet known in the art. See Allergy Asthma: Understanding

the causes and effects. <http://www.betterhealthcentre.com/allergy-asthma.htm> retrieved 26 February 2006, which teaches that the incidences of asthma have increased from 2-5% in 1959 to 38% in 1999, clearly demonstrating that asthma even now has not been prevented. The burden of enabling one skilled in the art to prevent all allergic diseases would be much greater than that of enabling the treatment of such diseases. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing allergic diseases. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for preventing allergic diseases.

No experimental evidence supporting the contention that the claim specified actives would actually prevent these diseases by simply administering the claim specified active agents has not been demonstrated nor practice the invention without an envisaged endpoint or result of the treatment (note the absence of such recitation in the current claim(s)). The specification fails to enable one of ordinary skill in the art to practice the presently claimed method for preventing and for practicing same without a specific endpoint for the treatment of the claimed diseases.

The term "prevention" or "preventing" is synonymous with the term "curing" and both circumscribe methods of treatment having absolute success. Since absolute success is not as of yet reasonably possible with most

diseases/disorders, especially those having etiologies and pathophysiological manifestations which are as complex/poorly understood as asthma for example.

4) the amount of direction or guidance presented; the specification does not provide any guidance in terms of preventing allergic diseases.

5) the presence or absence of working examples; no working examples are provided for preventing allergic diseases, for example in a patient, in the specification. The applicant has not provided any competent evidence or disclosed any tests that are highly predictive for the preventative effects of the instant composition. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

6) the quantity of experimentation necessary; the quantity of experimentation would be undue to one of skill in the art and amount to the trial and error type of experimentation without a priori expectation of success. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. To support a claim to prevention or the like, Applicant would need to provide confirmative in vivo data supporting the prevention of the disease as well as a method and dosage regime resulting in the prevention of same for a broad spectrum of patients.

In view of the breadth of the claims, the chemical nature of the invention and unpredictability of preventing cancer, and the lack of working examples regarding the activity as claimed, one skilled in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

In consideration of each of factors 1-8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

Claims 1-6 and 8-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

To satisfy the written description requirement, applicant must convey with reasonable clarity to one skilled in the art, as of the filing date that application was in possession of the claimed invention. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written

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description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

Possession may be shown in many ways. For example, possession may be shown by describing an actual reduction to practice of the claimed invention. Possession may also be shown by a clear depiction of the invention in detailed drawings or in structural chemical formulas which permit a person skilled in the art to clearly recognize that applicant had possession of the claimed invention. An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. For example, a specification may describe an actual reduction to practice by showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claim and determined that the invention would work for its intended purpose or an applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole.

An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with

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a known or disclosed correlation between function and structure, or some combination of such characteristics.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]."

Applicant has not conveyed possession of the invention with reasonable clarity to one skilled in the art. In particular, Applicant has not provided a description of the structure of a representative number of compounds nor a description of the chemical and/or physical characteristics of a representative number of compounds nor a description of how to obtain a representative number of specific compounds.

With regard to claims 10-15, Applicant has not provided sufficient working examples which would describe one of ordinary skill in the art an embodiment that met all the limitations of thereof. In other words, the Applicant has not described with sufficient clarity a method for agonizing activity to an EP3 receptor in all situations comprising each and every such compound. Absent a representative number of working examples coupled with for example, a clearly described common mechanism of action for example, the genus of compositions contemplated in claims 1-6 and 8-15 is not sufficient to provide predictable operability of the invention to one of ordinary skill in the art.

Claim Rejections - 35 USC § 112 – 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 and 8-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4 and 8-13 are of indeterminate scope. Defining a compound(s) by its (their) underlying functionality renders the description of same indeterminate since, the claim language may read on compounds not yet known or not yet understood. For example, a compound described herein as an EP3 agonist can be used in a method of treating alternative disorders such as those associated with the nervous system. Therefore, a description of an effective amount thereof, the objective of which condition

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is to be treated effectively, is variable. To that end, what success rate determines if a particular compound is effective and how many patients (and dosage regimens) need to be tested? The test for determining compliance with 35 USC 112, paragraph two, is whether applicants have clearly defined their invention, not what may be discovered by future research as this type of claim language clearly requires.

Claims 1-6, 9, 11-15 are further rejected under 35 U.S.C. 112, second paragraph, because the limitation "and/or" in line one of claim 1 for example is indefinite and can be interpreted to have alternative meanings such as "and" or "or".

Claim 10 provides for the use of a EP3 agonist, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

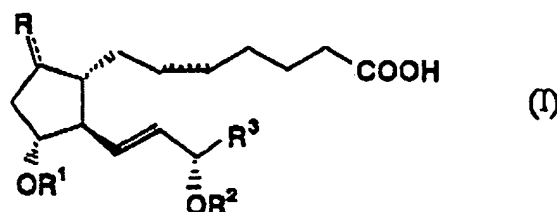
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 1008588 to Ono Pharmaceutical Co., Inc.

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The '588 reference discloses the a compound and pharmaceutical comprising a compound having the following general structure:



The recited use for the compound in the claims is of no moment in terms of patentability since the claims are directed to a composition.

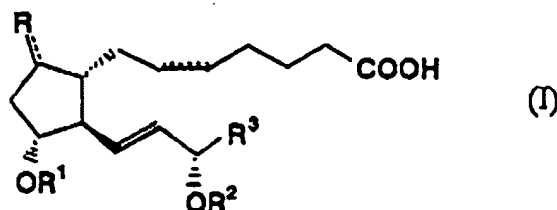
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6 and 8-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 1008588 to Ono Pharmaceutical Co., Inc. in view of Sheller et al. The prostaglandin E agonist, misoprostol, inhibits airway IL-5 production in atopic asthmatics. Prostaglandins & other Lipid Mediators 70 (2002) 185-193.

The '588 reference discloses the a compound and pharmaceutical comprising a compound having the following general structure:



The '588 reference does not teach that EP3 agonists are effective in treating allergies such as asthma.

Sheller et al. teach that misoprostol is effective in treating atopic asthma (in current claims 8-15; see Title) via signaling through the EP3 receptor (in current claims 8-15; see Discussion page 190).

One of ordinary skill in the art would have been motivated to combine the above references and as combined teach the claimed invention as claimed. One of ordinary skill in the art would have been motivated to combine the '588 reference and Sheller et al. because both are directed to agonizing EP3 and the inhibition of prostaglandin E2. Moreover, the selection of a known material based on its suitability for its intended use can support a prima facie obviousness determination and herein the teachings of Sheller et al. that agonizing PGE2 receptors such as EP3, results in a reduction of IL-5 and evidently eosinophils, mast cells and/or T lymphocyte production (all inflammatory cells), in light of the teaching in the '588 reference that EP3 is a recognized receptor for PGE2 makes a case of prima facie obviousness. Thus, the combined references teach and make prima facie obvious how to use the claimed invention at the time that it was made.

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Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michel Graffeo whose telephone number is 571-272-8505. The examiner can normally be reached on 9am to 5:30pm Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

12 April 2006
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